New Requirement for Electronic Submission of DMFs

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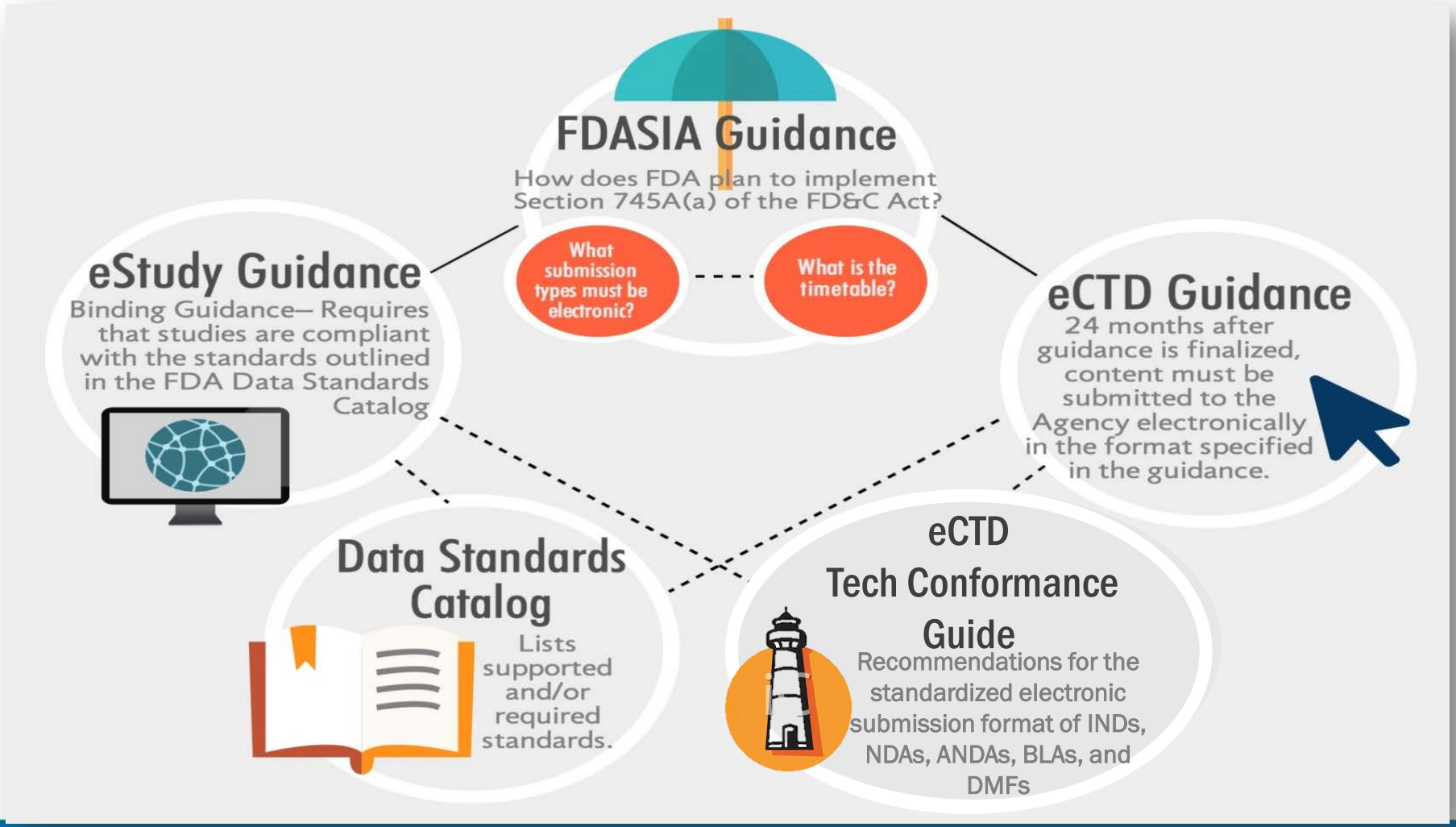
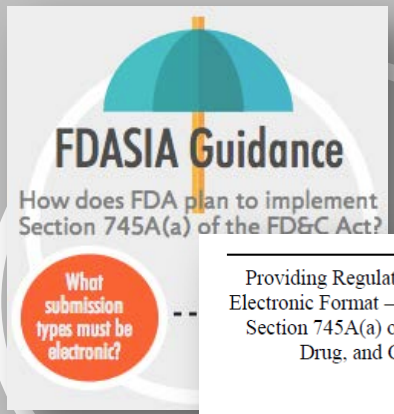
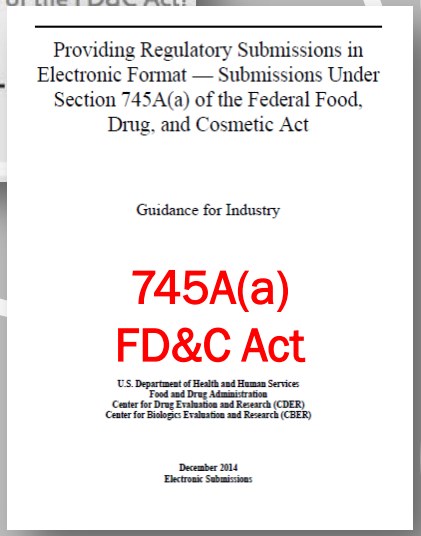
GPhA Fall Technical Conference
November 4, 2015 – North Bethesda, MD

Framework for Required Electronic Submissions



How will eSubmissions be Implemented?




Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

745A(a)
FD&C Act

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2014
Electronic Submissions

Final Published December, 2014

24 Months after Final Guidance

Individual Guidances

"745A(a) Umbrella" Implementation Guidance

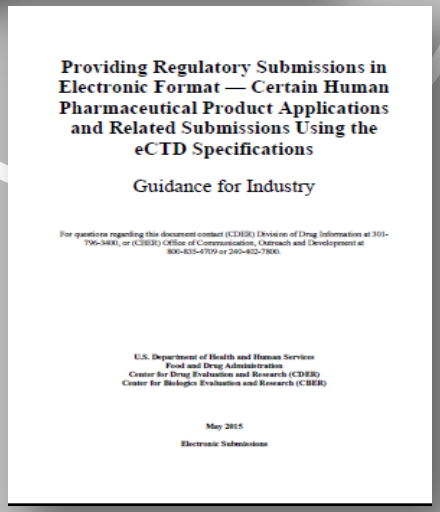
NDAs, ANDAs, BLAs, INDs

- Timetable
- Content
- Format

When will eCTD Format be Required?

eCTD Guidance

Binding Guidance requires the electronic submission of NDAs, BLAs, ANDAs, INDs, DMFs in eCTD Format



Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

Guidance for Industry

For questions regarding this document contact (CDER) Division of Drug Information at 301-796-3400, or (CBER) Office of Communication, Outreach and Development at 800-835-4709 or 240-402-7800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2015

Electronic Submissions

Published May 5, 2015

24 Months*

Required May 5, 2017

Compliance

Electronic submissions using the version of eCTD currently supported by FDA. As specified in the FDA Data Standards Catalog

*36 months for Commercial INDs

What Submission Types are Applicable?

eCTD Guidance

Binding Guidance requires the electronic submission of NDAs, BLAs, ANDAs, INDs, DMFs in eCTD Format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U.S. Department of Health and Human Services
Food and Drug Administration
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May 2015

Electronic Submissions

FDASIA Section 745A(a) applies to

Submissions under section 505(b), (i), or (j) of the FD&C Act

NDAs
ANDAs
BLAs
INDs
DMFs or BPFs
Combo products

Final Published May 5, 2015

When will eCTD Format be Required?

May 5, 2017

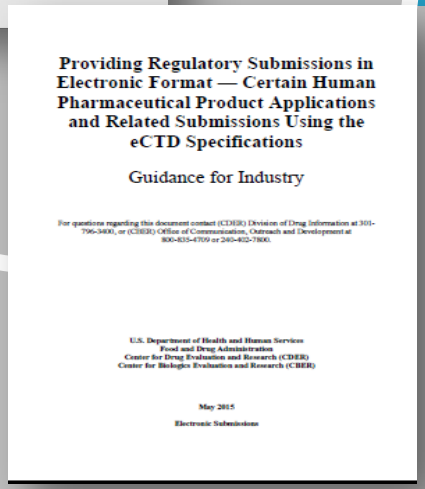
all DMF Submissions

must be in electronic, eCTD format

What are the eCTD Specifications?

eCTD Guidance

Binding Guidance requires the electronic submission of NDAs, BLAs, ANDAs, INDs, DMFs in eCTD Format



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May 2015

Electronic Submissions

Published
May 5, 2015

ICH eCTD Specs 3.2.2
ICH eCTD Study Tagging Files
FDA eCTD - Module 1
eCTD CTOC
Validation, File Format, PDF
Supportive files & more

Data Standards Catalog

Lists supported and/or required standards.

What eCTD Formats will be Required?

FDA Data Standards Catalog v4.1 (04-09-2015) - Supported and Required Standards

This table contains a listing of the data exchange, file formats and terminology standards supported at FDA. These standards have gone through all the steps necessary to make this part of the regulatory review process, including posting of regulatory guidance documents and associated implementation guidelines and technical specifications. The submission of standardized data using any standard not listed, or to an FDA Center not listed, should be discussed with the Agency in advance. This catalog is incorporated by reference in the guidance to industry, *Providing Regulatory Submissions in Electronic format-Standardized Study Data (http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf)*. A separate catalog will be published in the future that will contain a listing of standards that are in the development, testing, adoption or research & development (R&D) phases.

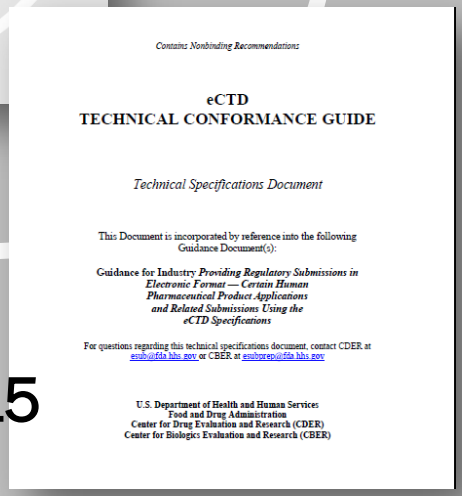
Use	Data Exchange Standard	Exchange Format	Standards Development Organization (SDO)	Supported Version	Implementation Guide Version	FDA Center(s)	Date Support Begins (MM/DD/YYYY)	Date Support Ends (MM/DD/YYYY)	Date Requirement Begins (MM/DD/YYYY)	Date Requirement Ends	Regulatory Reference and Information Sources
Regulatory Applications (IND, NDA, ANDA, BLA, master files)	Electronic Common Technical Document (eCTD)	Extensible Markup Language (XML)	International Conference on Harmonisation (ICH)	3.2.2	M2 eCTD: Electronic Common Technical Document Specifications	CDER, CBER	06/01/2008				Electronic Submissions-Electronic Common Technical Document (eCTD)
Product Labeling Submissions	Structured Product		Health Level 7			CDER,			04/01/2005 [3]		StructuredProductLabeling (SPL) Implementation Guide with Validation Procedures

How to Submit eCTD Submissions ?

Non-binding guidance

eCTD
Tech Conformance Guide

Recommendations for the standardized electronic submission format of INDs, NDAs, ANDAs, BLAs, and DMFs



Contains Nonbinding Recommendations

eCTD
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry ***Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications***

For questions regarding this technical specifications document, contact CDER at esub@fda.hhs.gov or CBER at esubprep@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

- General Considerations
- Organization of eCTD
  - Modules 1 -5
- Issues and Solutions

Published
October 5, 2015

Resubmission of Material

- There is NO requirement to resubmit anything that has already been submitted in paper
- *If you choose* to resubmit your entire DMF upon conversion to eCTD, that is acceptable but it is NOT required
- You may choose to use either version of eCTD Module 1 (DTD version 2.3 or 3.3)

eCTD Guidance

Binding Guidance requires the electronic submission of NDAs, BLAs, ANDAs, INDs, DMFs in eCTD Format

Will FDA Reject non-compliant submissions?

Yes.

eCTD Guidance

Binding Guidance requires the electronic submission of NDAs, BLAs, ANDAs, INDs, DMFs in eCTD Format

Waivers and Exemptions

Are there Waivers from the Requirement?

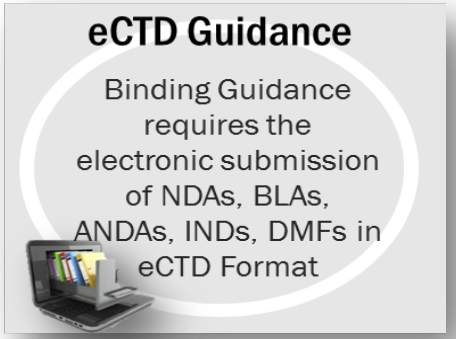
No.

Are there Exemptions from the Requirement?

Yes.

Types of Submissions Exempted

- INDs for
  - Non Commercial Products
    - Investigator-sponsored INDs
    - Expanded access INDs (e.g., emergency use INDs, treatment INDs)
- Blood and blood components, including Source Plasma
- Devices Regulated by CBER



*See the Guidance for a *complete* list of the "musts"*

- **Must** submit electronic submissions using the eCTD version currently supported by FDA.
  - The version of eCTD currently supported is specified in the Data Standards Catalog
- **Must** obtain a pre-assigned application number by contacting the appropriate Center.
- **Must** follow the FDA eCTD technical specification *Table of Contents Headings and Hierarchy.*

- **Must** adhere to the formats and versions specified in the FDA *Specifications for File Format Types Using eCTD Specifications*.
- **Must** adhere to the FDA *Portable Document Format (PDF) Specifications.*
- **Must** use the eCTD *replace* operation rather than submitting the file as *new* if a document replaces a document previously submitted …

- **Must** include only FDA fillable forms (e.g., 1571 or 356h) and electronic signatures to enable automated processing of the submission … *Scanned images of FDA forms will not be accepted.*
- **Must** not submit paper copies of the application, including review & desk copies when *submitting in eCTD format.*
- **Must** use the FDA Electronic Submission Gateway for submissions 10 GB or smaller.

Must use the FDA Electronic Submission Gateway (ESG) for submissions 10 GB or smaller

- If you are not currently an ESG submitter, set up an account now; process can take several weeks
- Most submitters use the “WebTrader Hosted Solution”
- There is no cost for an ESG account, but you must obtain a Digital Certificate for each person in your organization who will be sending files thru the ESG
- See the ESG website for complete instructions, http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm

Tips for DMF Submission Success

- Provide proper bookmarks, table of contents and hyperlinks on documents more than 5 pages long
- Pages should be properly oriented
- Scanned documents, including cover letters should be OCR'd prior to submitting
- Provide electronic submissions point of contact for technical issues
- Provide correct telephone, email or fax number for rejection notices
- Cover letter should always have US agent information should we need to contact sponsor

Tips for DMF Submission Success

- Leaf titles of documents should be clear and indicative of the document
- Cover letters should include the sequence number and if possible, date of submission (e.g. coverletter-0004-Oct-13-2015)
- Leaf titles for all annual report documents should include the reporting period (e.g. "AR-specifications-Oct-12-2014-Oct-11-2015). That way, reviewers can differentiate between one year's report from another.
- Do not include form 356h when submitting via gateway. DMFs are automatically processed without the form

Tips for DMF Submission Success

- Choose “CDER” as the center and “eCTD” as the submission type, when transmitting via ESG
- When transitioning from paper to eCTD and sponsor is utilizing v2.01 DTD, use “original-application” as the submission type. Subsequent submissions will be coded as “amendment”.
- When transitioning from paper to eCTD utilizing and sponsor is utilizing v3.3 DTD, the submission-Id should always be the same as the eCTD sequence number. (e.g. 0034-submission id-“original application”- sub-type-“application”-sequence number-“0034”; 0035-submission-id-“original application”- sub-type-“application”-sequence number-“0035).

Tips for DMF Submission Success

- Be sure to apply the correct metadata for m3.2.p and/or m3.2.s eCTD sections for every submission. Any minor change will add another 3.2.p. and/or 3.2.s section thus, creating duplicate sections
- Always apply the correct eCTD life cycle operator (e.g. replace) when submitting updates to documents. Do not submit updated documents as “new”

Remember ...

May 5, 2017

DMF Submissions

must be in eCTD format

Submissions 10GB and less must use the Gateway

Get an account NOW

Looking Forward to a Smooth Transition

Standardized electronic format = more efficient review process

References

- eCTD Web Page: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm
- Electronic Submissions Gateway: http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm
- Electronic Submissions Presentations: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm229642.htm
- Questions about submitting electronically to CDER: ESUB@fda.hhs.gov